



General

Guideline Title

Use of intensive insulin therapy for the management of glycemic control in hospitalized patients: a clinical practice guideline from the American College of Physicians.

Bibliographic Source(s)

Qaseem A, Humphrey LL, Chou R, Snow V, Shekelle P, Clinical Guidelines Committee of the American College of Physicians. Use of intensive insulin therapy for the management of glycemic control in hospitalized patients: a clinical practice guideline from the American College of Physicians. *Ann Intern Med.* 2011 Feb 15;154(4):260-7. [59 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

All American College of Physicians (ACP) clinical practice guidelines are considered automatically withdrawn or invalid 5 years after publication, or once an update has been issued.

Recommendations

Major Recommendations

The strength of the evidence (high, moderate, low, or insufficient evidence to determine benefits or risks) and strength of recommendations (strong, weak) are defined at the end of the "Major Recommendations" field.

Recommendation 1: *The American College of Physicians (ACP) recommends not using intensive insulin therapy to strictly control blood glucose in non-surgical intensive care unit/medical intensive care unit (SICU/MICU) patients with or without diabetes mellitus (Grade: strong recommendation, moderate-quality evidence).*

Current evidence does not show any reduction in mortality with a target blood glucose level of 4.4 to 10.0 mmol/L (80 to 180 mg/dL) compared with higher or unspecified targets using a variety of intensive insulin therapy (IIT) regimens for patients with myocardial infarction, stroke, or acute brain injury or those under perioperative care. A nonsignificant reduction in the incidence of infection has also been observed. Although the target blood glucose levels in the current trials ranged widely, avoiding targets less than 7.8 mmol/L (<140 mg/dL) should be a priority because harms are likely to increase at lower blood glucose targets. Although the consequences of hypoglycemia in hospitalized patients are unclear, there is some evidence for increased mortality or extended length of stay among patients experiencing 1 or more episodes of hypoglycemia. However, optimal targets in patients not receiving care in the SICU or MICU cannot be precisely defined, because IIT was associated with an excess risk for hypoglycemia in almost all trials and no clear differences in mortality were observed at any target level.

Recommendation 2: *ACP recommends not using intensive insulin therapy to normalize blood glucose in SICU/MICU patients with or*

without diabetes mellitus (Grade: strong recommendation, high-quality evidence).

Current evidence does not show a mortality benefit associated with use of IIT to achieve a target of normoglycemia (blood glucose levels of 4.4 to 6.1 mmol/L [80 to 110 mg/dL]). Evidence from some studies showed an increase in mortality associated with IIT and hypoglycemia. Data on the effects of IIT targeted to normoglycemia on reduction in length of ICU stay are mixed.

Recommendation 3: *ACP recommends a target blood glucose level of 7.8 to 11.1 mmol/L (140 to 200 mg/dL) if insulin therapy is used in SICU/MICU patients* (Grade: weak recommendation, moderate-quality evidence).

Although IIT to achieve targeted normoglycemia is not associated with improved health outcomes and increases the risk for hypoglycemia, poorly controlled hyperglycemia is associated with increased morbidity, mortality, and worsened health outcomes in patients in the ICU. While the evidence is not sufficient to give a precise range for blood glucose levels, target values of 7.8 to 11.1 mmol/L (140 to 200 mg/dL) is a reasonable option in patients in the ICU, because insulin therapy targeted at blood glucose levels of 7.8 to 11.1 mmol/L (140 to 200 mg/dL) is associated with similar mortality outcomes as IIT targeted at blood glucose levels of 4.4 to 6.1 mmol/L (80 to 110 mg/dL) and is associated with a lower risk for hypoglycemia. Current studies do not provide enough information to determine whether allowing blood glucose levels to increase above 10.0 to 11.1 mmol/L (180 to 200 mg/dL) is associated with similar outcomes to those seen at lower target levels.

Although the risk for hypoglycemia was higher in studies with lower target glucose values, hypoglycemia was also observed among patients who received insulin therapy with target blood glucose levels ranging from 7.8 to 11.1 mmol/L (140 to 200 mg/dL). Therefore, minimizing hypoglycemia associated with IIT is critical in institutions that choose to implement insulin therapy in patients in the ICU. Factors that may be associated with achievement of glucose targets with low rates of hypoglycemia include titration characteristics of the protocol, patient characteristics, staffing ratios, and clinician acceptance. Institutions that implement insulin therapy in patients in the ICU should incorporate quality improvement and training initiatives in order to achieve target glucose levels while minimizing rates of hypoglycemia.

Definitions:

The American College of Physicians' Guideline Grading System*		
Quality of Evidence	Strength of Recommendation	
	Benefits Clearly Outweigh Risks and Burden or Risks and Burden Clearly Outweigh Benefits	Benefits Finely Balanced With Risks and Burden
High	Strong	Weak
Moderate	Strong	Weak
Low	Strong	Weak
Insufficient evidence to determine net benefits or risks		

*Adopted from the classification developed by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) workgroup.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Inpatient hyperglycemia

Note: Hyperglycemia is associated with poor immune response, increased cardiovascular events, thrombosis, inflammatory changes, delayed

healing, and other problems.

Guideline Category

Management

Treatment

Clinical Specialty

Endocrinology

Internal Medicine

Intended Users

Physicians

Guideline Objective(s)

- To present the evidence for the link between the use of intensive insulin therapy to achieve different glycemic targets and health outcomes in hospitalized patients with or without diabetes mellitus.
- To address the management of hyperglycemia and evaluate the benefits and harms associated with the use of intensive insulin therapy (IIT) to achieve tight glycemic control in hospitalized patients with or without diabetes mellitus.
- To present the evidence for the following questions:
 - Does the use of IIT to achieve tight glycemic control compared with less tight glycemic control improve important health outcomes in the following settings or patient populations: surgical intensive care unit (SICU), medical intensive care unit (MICU), general surgical ward, general medicine ward, patients with myocardial infarction or acute stroke, and patients in the perioperative setting?
 - What are the harms of strict glycemic control in the above subpopulations?

Target Population

Adults with inpatient hyperglycemia in a hospital setting

Interventions and Practices Considered

Intensive insulin therapy

Major Outcomes Considered

- Short-term mortality
- Hypoglycemia

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The databases used for the literature search were MEDLINE and the Cochrane Database of Systematic Reviews; the search included studies published from database inception through January 2010. The literature search was supplemented by reviews of reference lists, suggestions from consulting experts, and searches on ClinicalTrials.gov for unpublished studies. Each article was reviewed by using the eligibility criteria outlined in the systematic review. Eligible articles were published in English and provided primary data relevant to the use of intensive insulin therapy (IIT) in hospitalized patients. Studies evaluating fixed-dose insulin infusions, including trials of fixed-dose glucose-insulin-potassium infusions, were excluded.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

This guideline rates the evidence and recommendations by using the ACP guideline grading system, which is based on the system developed by the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) workgroup (see the "Rating Scheme for the Strength of the Recommendations" field).

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

Description of the Methods Used to Analyze the Evidence

The quality of each study was rated as good, fair, or poor on the basis of 1) the comparability of treatment groups; 2) the adequacy of randomization; 3) whether treatment allocation was concealed; 4) whether eligibility criteria were specified; 5) whether patients, care providers, and outcome assessors were blinded; 6) whether the analysis was done on an intention-to-treat basis, conducted with postrandomization exclusions, or had extensive or differential loss to follow-up; and 7) whether clearly defined interventions and reliable outcome measurement were used. Given the importance of glucose control and hypoglycemia in assessing the effectiveness and safety of intensive insulin therapy (IIT), studies that did not fully report glucose levels achieved or overall hypoglycemia rates were rated as poor quality.

Three investigators reviewed the abstracts of citations identified from literature searches. When reviewers disagreed about the quality rating, consensus was reached through discussion with all authors. Details of the methods for the evidence review are provided in the evidence review (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Not stated

Rating Scheme for the Strength of the Recommendations

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Low	Strong	Weak
Insufficient evidence to determine net benefits or risks		

*Adopted from the classification developed by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) workgroup.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

This guideline was approved by the American College of Physicians (ACP) Board of Regents on 20 November 2010.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate use of intensive insulin therapy (ITT) for the management of glycemic control in hospitalized patients

Potential Harms

- Intensive insulin therapy (IIT) was associated with an excess risk for hypoglycemia in almost all trials and no clear differences in mortality were observed at any target level.
- Evidence from some studies showed an increase in mortality associated with IIT and hypoglycemia.

Qualifying Statements

Qualifying Statements

- Clinical practice guidelines are "guides" only and may not apply to all patients and all clinical situations. Thus, they are not intended to override clinicians' judgment.
- The authors of this article are responsible for its contents, including any clinical or treatment recommendations. No statement in this article should be construed as an official position of the U.S Department of Veterans Affairs.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Mobile Device Resources

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

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intensive insulin therapy for the management of glycemic control in hospitalized patients: a clinical practice guideline from the American College of Physicians. *Ann Intern Med.* 2011 Feb 15;154(4):260-7. [59 references] [PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2011 Feb 15

Guideline Developer(s)

American College of Physicians - Medical Specialty Society

Source(s) of Funding

American College of Physicians

Guideline Committee

Clinical Guidelines Committee of the American College of Physicians

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Any financial and nonfinancial conflicts of interest of the group members were declared, discussed, and resolved. Dr. Vincenza Snow was an employee of the American College of Physicians at the time of the writing of this guideline. Dr. Snow: *Employment:* American College of Physicians, Pfizer. Dr. Shekelle: *Grants/grants pending (money to institution):* Agency for Healthcare Research and Quality; *Royalties:* UpToDate. Disclosures can also be viewed at <https://www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M10-2725>

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Guideline Availability

Electronic copies: Available from the [Annals of Internal Medicine Web site](#) .

Print copies: Available from Amir Qaseem, MD, PhD, MHA, American College of Physicians (ACP), 190 N. Independence Mall West, Philadelphia PA. email: aqaseem@acponline.org

Availability of Companion Documents

The following are available:

- Qaseem A, Snow V, Owens DK, Shekelle P. The development of clinical practice guidelines and guidance statements of the American College of Physicians: summary of methods. Ann Intern Med. 2010 Aug 3;153(3):194-199. Electronic copies: Available from the [Annals of Internal Medicine Web site](#) .
- Kansagara D, Fu R, Freeman M, Wolf F, Helfand M. Systematic review: intensive insulin therapy in hospitalized patients. Ann Intern Med. 2011;154:268-282. Available from the [Annals of Internal Medicine Web site](#) .

Print copies: Available from the American College of Physicians (ACP), 190 N. Independence Mall West, Philadelphia PA 19106-1572.

A collection of Recommendation Summaries for all current American College of Physicians (ACP) Clinical Guidelines is now available for mobile devices from the [ACP Web site](#) .

A continuing medical education (CME) course is also available from the [Annals of Internal Medicine Web site](#) .

Patient Resources

None available

NGC Status

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